

### REMARKS

This Supplemental Amendment and Response is being submitted in response to the Office Communication (Response to Amendment) mailed on January 27, 2005. In the Response to Amendment, the Examiner objects to the format of the Amendment to the claims filed on October 25, 2004. Specifically, the Examiner states that the applicants have not provided an accurate marked up version of the amended claims, *i.e.*, some of the language of the claims in the Amendment, which is indicated as the language of the claims as filed, is not present in the claims as filed.

Based on the telephone conversation with the Examiner on February 28, 2005, applicants understand that the Amendment and Response filed on October 25, 2004 have not been entered. Accordingly, applicants request entry of the present Supplementary Amendment and Response in place of the Amendment and Response filed on October 25, 2004.

Applicants respectfully note that, as follows from the Examiner's statements in the Response to Amendment mailed on January 27, 2005, the Examiner is mistaken in his belief as to the identity of the claims as filed in the present application. Applicants respectfully note that the present U.S. patent application is a National Phase (§371) of the PCT Application No. PCT/US00/19239, filed on July 14, 2000. Accordingly, the present application as filed should be the application transmitted by the International Bureau. Applicants further note that the claims as filed in the present U.S. application should be identical to the claims attached to the International Preliminary Examination Report entered by the Examining Authority (mailed on November 6, 2001; copy attached as Exhibit A). These claims are not identical to the claims originally filed in the PCT application but correspond to the claims as amended in the Response to Written Opinion filed on August 13, 2001.

However, applicants further note that the deleted language in claims 3, 4 and 13 as presented in the Amendment filed on October 25, 2004 did not correctly represent the language of these claims as filed in the present application. Specifically, the word “of” was missing after the word “catalysis” in line 2 of claim 3; the word “enzyme” was missing after the word “prothrombinase” in line 2 of claim 4; the phrase “is an exogenous prothrombinase” was



prothrombinase. In response, without conceding the validity of the rejections, claims 1-3 have been amended. The amended claims are directed to “a method for assaying activation state of platelets,” comprising steps (a) and (b), as set forth in claim 1. The amendments to claims 1-3 are believed to address and overcome the basis of the rejections. Reconsideration of claims 1-3 and withdrawal of all rejections thereof under 35 U.S.C. § 112, first paragraph for lack of enablement is requested, accordingly.

(ii) *(i) Rejections Under 35 U.S.C. § 112, second paragraph.* Claims 1-12 have been rejected as allegedly indefinite for including the term “detecting.” The Examiner’s position is that it is not known what catalytic entity is to undergo or receive “detecting.” In response, without conceding the validity of the rejections or the Examiner’s position, the claims 1-8, 11 and 12 have been amended. Claims 9 and 10 have been canceled.

Claims 1-8, 11, and 12 are now directed to a method for assaying platelet activation state. The method comprises providing a mixture comprising platelets, a prothrombin-converting enzyme, and a substrate for the prothrombin-converting enzyme, and assaying the production of a product produced in the mixture, which product does not activate platelets (see amended claim 1). Each of claims 2-8, 11, and 12 depend either directly or indirectly from claim 1 and are therefore, likewise, directed to a method comprising providing a mixture comprising platelets, a prothrombin-converting enzyme, and a substrate for the prothrombin-converting enzyme, and assaying the production of a product produced in the mixture, which product does not activate platelets. The basis of the present rejection of remaining claims 1-8, 11, and 12 is therefore believed to have been addressed and overcome.

The Examiner has objected to the term “associated” in claim 1. In response, without conceding the validity of the Examiner’s position, claim 1 has been amended. The phrase “a prothrombinase which is associated with the platelet” does not appear in the amended claim. The basis of the present rejection is believed to have been addressed and overcome.

The Examiner has objected to recitation of the phrase “modified prothrombinase substrate” that appeared in claims 1-3, 5-7, 13, 15, and 16. In response, without conceding the validity of the Examiner’s position, the claims have been amended and are now directed, in



In making the rejection, the Examiner disregards the express definitions of “modified prothrombin” and “modified thrombin,” as well as “prothrombinase substrate” (e.g., prothrombin) and “prothrombinase product” (e.g., thrombin) in the specification (page 7, lines 1-25). Nothing in the references suggests that the thrombin disclosed therein fails to activate platelets.

Indeed, the prothrombin and thrombin molecules described in the reference is not modified in the context of any definition. The reference merely describes that aspirin depresses thrombin formation in clotting blood and goes on to state, “It is suggested that aspirin exerts this effect by acetylating prothrombin and/or macromolecules of platelet membrane.” (Szczeklik et al., Abstract, emphasis added). According to the reference, however, the mechanism by which aspirin acts is “unknown.” Szczeklik et al. at page 2010, col. 1, line 25-26. Hence, there is no evidence that Szczeklik et al. react a modified prothrombin with prothrombinase. Nor, in any event, do Szczeklik et al. describe assaying for any prothrombinase product other than thrombin.

In view of the foregoing, Szczeklik et al. does not anticipate the claimed invention. Where a reference fails to teach an element of an invention, it cannot anticipate that invention. Reconsideration of pending claims 1-5, 10, 11, 13, 15, 17, and 19-20 and withdrawal of the rejection thereof under 102(b) is requested, accordingly.

(iv) Rejections Under 35 U.S.C. § 103. Claims 8 and 14 are rejected as allegedly obvious over Szczeklik et al. in view of Phizicky & Fields, 59 Microbiol. Rev. 94 (1995) (“Phizicky & Fields”). Claims 12, 14, and 18 are rejected as allegedly obvious over Szczeklik et al. in view of Mattler & Bang, Thromb. Haemost. 38:776 (1977) (“Mattler & Bang”). The rejections are respectfully traversed, as follows.

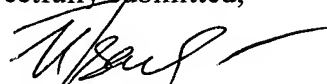
In making the obviousness rejections, the Examiner relies on Szczeklik et al. as the primary reference. Each of the rejected claims is directed to production and assay of a modified prothrombinase product which does not activate platelets. (See: Claim 1, base claim for claims 8 and 12; claim 13, base claim for claims 14 and 18.) As discussed above, Szczeklik et al. fails to disclose a method comprising converting a prothrombinase substrate to a modified prothrombinase product which does not activate platelets and assaying the presence of the



hereby authorized to charge any additional fees associated with this response to our Deposit Account No. 04-0100.

Respectfully submitted,

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